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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/819,371	03/28/2001	Kohji Egawa	31508	4334

7590 07/28/2005

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 07/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/819,371	EGAWA, KOHJI	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 60-72 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 60-72 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 2/3/04+7/30/01.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 39-59 have been canceled. Claims 60-72 have been added and are under consideration.

2. Sections of Title 35, U.S. Code not found in this action, can be found in a previous action.

3. Claim 39 is objected to because of the following informalities: the typographical error of cancer "call" rather than cancer cell. Appropriate correction is required.

4. Claims 60-72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(A)The recitation of "the cancer" in the last line of claims 60, 68, 69 and 71 lacks antecedent basis within the claims, and does not related to the method objective which is specifically drawn to the diagnosis of "a" cancer.

(B) Claims 60, 61, 68, 69, 70, 71 and 72 recite an amino acid sequence or DNA sequence corresponding to SEQ ID NO:X. The metes and bounds of "corresponding to" a sequence are unclear as it is unknown whether "corresponding to" allows for deviations from the recited amino acid sequence. Further, it is unclear if "an amino acid sequence of" is referring to fragments of the SEQ ID NO rather than the sequence in its entirety.

(C) Claims 39, 50 and 59 fail to relate the detection of the antigen-antibody complex with the diagnosis of cancer. The last active method step is the detection of the labeled secondary antibody reacted with the immune complex, but not connection is made between this detection and the diagnosis of cancer.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 60-72 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

(A) As drawn to inadequate written description

The instant method claims are reliant upon the identity of the HLA-F antigen. The specification states that the *"HLA-F antigen, as the primary substance of the present invention, may be any antigen, as long as it binds as an antigen to an anti-HLA-F antibody in body fluid; specifically, said antigen comprises a part of the amino acid sequence described in SEQ ID No. 4 in the Sequence Listing. To be more specific, it contains at least an amino acid sequence in SEQ ID No. 5 and, preferably, at least an amino acid sequence in SEQ ID No. 6. Or, as long as it binds as an antigen to an anti-HLA-F antibody, it may be a part or an entirety of the amino acid sequence in SEQ ID No. 5 in the Sequence Listing or a part or an entirety of the amino acid sequence in SEQ ID No. 6. Amino acid sequences may be partially replaced, deleted, or added of a few amino acids by polymorphism in the species or by mutation without causing changes in their essential characteristics and; therefore, the claim of the present invention extends over such sequences, as long as they exert no fundamental modifications to the nature of the invention"* (page 6, line 20 to page 7, line 16). Thus, the definition of the HLA-F antigen permits deviation from the amino acid sequence of HLA-F, and requires only that the resulting antigen binds to an anti-HLA-F antibody in body fluid. The reliance on binding to "an HLA-F antibody" to define the structural limitations for an HLA-F antigen does not impart structural constraints on said antigen, because the binding ability of an antibody is the result of the structure of the protein to which it binds. It said structure is variant, then the antibody raised against said structure will also be variant. Further, the claims recite "an amino acid sequence corresponding to" a particular SEQ ID NO and when given the broadest reasonable interpretation, this includes fragments of the SEQ ID NO as well homologues of the SEQ ID NO.

Claim 68 requires "at least a part of an amino acid sequence corresponding to SEQ ID NO:6". When given he broadest reasonable interpretation, "at least a part" of an amino acid sequence is a single amino acid. Thus, the claims are not limited by the structure of a particular antigen. The specification provide a written description of the HLA-F antigen as comprising SEQ ID NO:5 or SEQ ID NO:6. This disclosure does not adequately described the genus relied upon in the instant claims because said genus is highly variant, tolerating widely variant structural deviations from the of amino acids comprising SEQ ID NO:5 or 6. One of skill in the art would reasonable conclude that applicant was not in possession of the genus of HLA-F antigens a the time of filing. It logically follow that if a product is not adequately described, the method of using said product is also not adequately described.

(B) As drawn to new matter

Claim 68 is a method reliant on the identify of the HLA-F antigen characterized as having a molecular weight selected from 29, 25, 18 or 13 KDa. The specification as filed states that the antigen has a molecular weight of 31, 29, 18 or 13 Kda. This does not provide support for a 25 Kda antigen.

7. Applicant argues that the HLA-F antigen is adequately described by the specification, citing text wherein the molecular weight and SEQ ID NO is set forth. However, this is not persuasive, because the specification defines the HLA-F antigen as encompassing variants of HLA-F, and that said variants need only comprise a portion of the disclosed SEQ ID NO, which for the reasons stated above, encompass a large variant genus of proteins which are not adequately described by proteins comprising the entirety of SEQ ID NO:6 or 5.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 60-64 and 68-72 are rejected under 35 U.S.C. 102(b) as being anticipated by Stockert et al (WO99/53938)

Claim 60 is drawn to a method of diagnosing a cancer that is non-specific to various organs comprising the steps of contacting a cancer cell specific HLA-F antigen which comprises an amino acid sequence corresponding to SEQ ID NO:6 with a body fluid of a subject; reacting the HLA-F antigen with a HLA-F antibody in said body fluid to form an immune complex; applying a secondary antibody to the immune complex in the body fluid, said secondary antibody bind labeled; reacting the labeled secondary antibody with the immune complex in the body fluid; detecting the labeled antibody with the immune complex by using the lab le and diagnosing the subject as having [the] cancer. Claim 61 embodies the method of claim 60 wherein the cancer cell specific HLA-F antigen is obtained by expressing a DNA sequence corresponding to SEQ ID NO:3. Claim 62 embodies the method of claim 60 wherein the body fluid is serum. Claim 63 embodies the method of claim 60 wherein the labeled antibody is selected from the group consisting of an anti-human IgG rabbit antibody, an anti-human IgG mouse antibody, and an anti-human IgG goat antibody. Claim 64 embodies the method of claim 60 wherein the cancer is selected from the group consisting of liver, stomach, uterine, breast, pancreatic and ovarian.

Claim 68 is drawn to a method of diagnosing a cancer that is nonspecific to various organs comprising the steps of contacting a cancer cell specific HLA-F antigen with a body fluid of a subject, said antigen having a molecular weight selected from the group consisting of 29kD, 25kD, 18kD, or 13kD and which comprises at least a part of the amino acid sequence corresponding to SEQ ID NO:6; reacting the HLA-F antigen with a HLA-F antibody in the body fluid to form an immune complex; applying a secondary labeled antibody to the immune complex; detecting the labeled immune complex and diagnosing the subject as a patient having [the] cancer.

Claim 69 is drawn to a method of diagnosing a cancer that is nonspecific to various organs comprising the steps of contacting a cancer cell specific HLA-F antigen comprising at least an amino acid sequence corresponding to SEQ ID NO:5 with a body fluid of a subject; reacting the HLA-F antigen with a HLA-F antibody in the body fluid to form an immune complex; applying a secondary labeled antibody to the immune complex; detecting the labeled immune complex and diagnosing the subject as a patient having [the] cancer. Claim 70 embodies the method of claim 69 wherein the cancer cell specific HLA-F antigen is obtained by

expressing a DNA sequence which comprises at least the DNA sequence corresponding to SEQ ID NO:2.

Claim 71 is drawn to a method of diagnosing a cancer that is nonspecific to various organs comprising the steps of contacting a cancer cell specific HLA-F antigen with a body fluid of a subject, said antigen, comprising at least an amino acid sequence corresponding to SEQ ID NO:4; reacting the HLA-F antigen with a HLA-F antibody in the body fluid to form an immune complex; applying a secondary labeled antibody to the immune complex; detecting the labeled immune complex and diagnosing the subject as a patient having [the] cancer. Claim 72 embodies the method of claim 71 wherein the cancer cell specific HLA-F antigen is obtained by expressing a DNA sequence which comprises at least a DNA sequence corresponding to SEQ ID NO:1.

Stockert et al disclose a method of detecting cancer comprising detecting antibodies to NY-ESO-1 in patient serum using an detectable labeled goat anti-human antibody (page 9, line 1 to page 11, line 14, claims 81 and 94). Stockert et al disclose that patients with melanoma, breast, lung and ovarian cancers had antibodies to NY-ESO-1 in their sera, but that normal individuals did not have said antibodies. Stockert et al disclose that the NY-ESO-1 antigen has a molecular weight of 17,995 Dalton, thus fulfilling the specific embodiments of claim 68. Because the metes and bound of "sequence corresponding to" a given SEQ ID NO cannot be determined, and because the specification defines the HLA-F antigen as encompassing HLA-F wherein amino acids are replaced, deleted, or added, and because the only functional characteristic given for the HLA-F antigen is that it binds to the HLA-F antibody, no structural limitations can be imparted by the recitation of "an amino acid sequence corresponding to" a given SEQ ID NO, because an antibody can only be structurally defined if the protein to which it binds is structurally defined, In the instant case, the HLA-F protein is defined as including variant HLA-F sequences. Therefore the binding to the HLA-F antibody has no independent meaning and does not impart structural characteristics to the variant proteins. Further, claim 68 requires "at least part" of the amino acid sequence corresponding to SEQ ID NO:6. A "part" of an amino acid sequence can be construed to mean a single amino acid, Claims 70 and 72 do not limit the structure of the HLA-F antigen for the same reasons regarding the recited sequences, and further, because they are product by process claims. The M.P.E.P. (2113) states

PRODUCT-BY-PROCESS CLAIMS ARE NOT LIMITED TO THE MANIPULATIONS OF THE RECITED STEPS, ONLY THE STRUCTURE IMPLIED BY THE STEPS

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

Thus, as long as the HLA-F antigen satisfies the limitations of claims 69 and 71, the dependent claims 70 and 72 do not serve to further limit claims 69 and 71.

10. Claims 60-62, 64-67 and 69-72 are rejected under 35 U.S.C. 102(b) as being anticipated by Hashizume et al (5,094,942).

The specific embodiments of the claims are recited above. Hashizume et al disclose a method of detecting cancer comprising detecting an antibody in the serum of patients which binds to immobilized animal carboxypeptidase by means of a labeled anti-human IgG or IgM (claim 1). Hashzume et al disclose that cancers of the lung, ovary, larynx, uterus, liver, rectum and stomach can be detected by this method, thus fulfilling the specific embodiments of claims 65-67).

11. Claims 60-67 and 69-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hashizume et al (5,094,942) in view of The Sigma Catalog (1997, p1347-1351).

Claim 63 embodies the method of claim 60 wherein the labeled secondary antibody is a anti-human IgG rabbit, mouse or goat antibody.

Hashizume et al teach a generic anti-human IgG or IgM antibody; Hashizume et al do not specifically teach a rabbit, mouse or goat anti-human IgG.

The Sigma Catalog teaches mouse and goat anti-human IgG conjugates which carrying a detectable label.

It would have been prima facie obvious at the time the claimed invention was made to use a mouse anti-human IgG antibody. One of skill in the art would have been motivated to do so by the avaiability of the specific labeled antibodies taught by the Sigma Catalog to react with human IgG.

All other rejections and objections as set forth or maintained in the previous Office action are withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 11 am to 10 pm, except Wed, Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
7/25/2005

KAREN A. CANELLA PH.D
PRIMARY EXAMINER